

**IN THE DRAWINGS:**

The attached drawings include changes to FIGs. 1, 2A, 2B, 4A-4C, 5A-5C, and 6A-6C. The sheets containing FIGs. 1, 2A-2B, 4A-4C, 5A-5C, and 6A-6C replace the original sheets including FIGs. 1, 2A-2B, 4A-4C, 5A-5C, and 6A-6C. The changes to the drawings are described below.

In FIG. 1, the reference numeral for the syringe (piston) assembly has been changed from "113" to "112" and the short tube 113 has been identified to correspond to the specification. Reference numerals 104 and 106 have also been added to correspond to the specification.

In FIG. 2A, reference numerals 102, 106, and 113 have been added to correspond to the specification. The reference numeral for the bore has been changed from "103" to "104," the reference numeral for the lens has been changed from "107" to "108," and the reference numeral for the filter has been changed from "102" to "107" to correspond to the specification.

In FIG. 2B, reference numerals 107, 108, 130, 160, 161, and 170 have been added to correspond to the specification.

FIG. 4A has been relabeled from "4A" to "FIG. 4A" for clarity and "veiw" has been corrected to "view."

FIG. 4B has been relabeled from "4B" to "FIG. 4B" for clarity and "veiw" has been corrected to "view."

FIG. 4C has been relabeled from "4C" to "FIG. 4C" for clarity.

FIG. 5A has been relabeled from "A" to "FIG. 5A" for clarity, "Reservour" has been corrected to "reservoir," and the reference numeral for the plug/matrix has been changed from "141" to "132" to correspond to the specification.

FIG. 5B has been relabeled from "B" to "FIG. 5B" for clarity and reference numeral 131 has been added to correspond to the specification.

FIG. 5C has been relabeled from "C" to "FIG. 5C" for clarity.

FIG. 6A has been relabeled from "A" to "FIG. 6A" for clarity, and bore tube 151 and tube end 153 have been correctly identified to correspond to the specification.

FIG. 6B has been relabeled from "B" to "FIG. 6B" for clarity and tube end 157 has been correctly identified to correspond to the specification.

FIG. 6C has been relabeled from "C" to "FIG. 6C" for clarity and reference numerals 108, 171, and 200 have been added to correspond to the specification.

No new matter has been added. Approval of these changes to the Drawings is respectfully requested.

**REMARKS**

Claims 7-12, 15, and 17-20 are pending in this application. Claims 7 and 12 are independent claims. Claims 8-11, 15, and 17-20 are dependent claims.

Claims 7-12, 15, and 17-20 have been rejected. Amendments to claims 7, 12, 15, and 18 are presented herein.

The drawings and specification have been amended to improve form. No new matter is being presented, and approval and entry are respectfully requested.

**Changes to the Drawings**

The attached drawings include changes to FIGs. 1, 2A, 2B, 4A-4C, 5A-5C, and 6A-6C. The sheets containing FIGs. 1, 2A-2B, 4A-4C, 5A-5C, and 6A-6C replace the original sheets including FIGs. 1, 2A-2B, 4A-4C, 5A-5C, and 6A-6C. The changes to the drawings are described below.

In FIG. 1, the reference numeral for the syringe (piston) assembly has been changed from "113" to "112" and the short tube 113 has been identified to correspond to the specification. Reference numerals 104 and 106 have also been added to correspond to the specification.

In FIG. 2A, reference numerals 102, 106, and 113 have been added to correspond to the specification. The reference numeral for the bore has been changed from "103" to "104," the reference numeral for the lens has been changed from "107" to "108," and the reference numeral for the filter has been changed from "102" to "107" to correspond to the specification.

In FIG. 2B, reference numerals 107, 108, 130, 160, 161, and 170 have been added to correspond to the specification.

FIG. 4A has been relabeled from "4A" to "FIG. 4A" for clarity and "veiw" has been corrected to "view."

FIG. 4B has been relabeled from "4B" to "FIG. 4B" for clarity and "veiw" has been corrected to "view."

FIG. 4C has been relabeled from "4C" to "FIG. 4C" for clarity.

FIG. 5A has been relabeled from "A" to "FIG. 5A" for clarity, "Reservoir" has been corrected to "reservoir," and the reference numeral for the plug/matrix has been changed from "141" to "132" to correspond to the specification.

FIG. 5B has been relabeled from "B" to "FIG. 5B" for clarity and reference numeral 131 has been added to correspond to the specification.

FIG. 5C has been relabeled from "C" to "FIG. 5C" for clarity.

FIG. 6A has been relabeled from "A" to "FIG. 6A" for clarity, and bore tube 151 and tube end 153 have been correctly identified to correspond to the specification.

FIG. 6B has been relabeled from "B" to "FIG. 6B" for clarity and tube end 157 has been correctly identified to correspond to the specification.

FIG. 6C has been relabeled from "C" to "FIG. 6C" for clarity and reference numerals 108, 171, and 200 have been added to correspond to the specification.

No new matter has been added. Approval and entry of the attached replacement sheets are respectfully requested.

#### Changes To The Specification

Changes have been made to the specification only to place it in preferred and better U.S. form for issuance. No new matter has been added.

#### Objections to the Claims

In numbered paragraphs 2 and 3 on page 2 of the Office Action, the Examiner objected to claims 15 and 18 because of various informalities. Applicants submit that amendments to the claims presented above correct the informalities. Accordingly, Applicants respectfully request withdrawal of the objections to claims 15 and 18.

**Rejections Under 35 U.S.C. § 112, First Paragraph**

In numbered paragraph 5 on pages 2 and 3 of the Office Action, the Examiner rejected claims 7-12, 15, and 17-20 under 35 U.S.C. §112, first paragraph, as not being enabling for the reasons set forth therein.

The Examiner stated that there is no teaching of how the components (a light source, a sample holder, and a detector) can be used in an in vivo setting, and that the term "in vivo" in the preamble of independent claims 7 and 12 is considered to be new matter. Applicants point out that the term "in vivo" was part of claim 7 as originally filed and, thus, should not be considered new matter. Also, FIGs. 4A to 4C and pages 6, 7, and 19 of the specification describe an embodiment of the present invention for detecting target molecules in whole, live eels. Accordingly, Applicants respectfully request withdrawal of the rejection to the claims under § 112, first paragraph.

**Rejections Under 35 U.S.C. § 112, Second Paragraph**

In numbered paragraphs 8 and 9 on page 3 of the Office Action, the Examiner rejected claims 7 and 12 as being indefinite for using the terms "the molecule" and "a capture molecule." Claims 7 and 12 have been amended to distinguish between a "target molecule" and a "capture molecule." Applicants submit that the amendments to the claims presented above meet the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejections to claims 7 and 12 under § 112, second paragraph.

In numbered paragraph 10 on page 4 of the Office Action, the Examiner rejected claim 12 as being indefinite for the reasons set forth therein. Claim 12 has been amended to delete the multiple occurrence of "an analysis target area." Applicants submit that the amendments to the claims presented above meet the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection to claim 12 under § 112, second paragraph.

In numbered paragraph 11 on page 4 of the Office Action, the Examiner rejected claim 15 as being indefinite for the reasons set forth therein. Claims 12 and 15 have been amended to clarify the locations of the uptake channel and the analysis target area. Applicants submit

that the amendments to the claims presented above meet the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection to claim 15 under § 112, second paragraph.

In numbered paragraph 12 on page 4 of the Office Action, the Examiner rejected claim 18 as being indefinite. The Examiner stated that it is unclear whether the laser dye binds to albumin, lipoproteins, and gamma globulins at once or whether the phrase includes a Markush grouping. Multiple dyes can be used in one organism and the dyes can bind to different proteins. Therefore, any combination of the three proteins can be used as part of different tags to provide different information. For example, one of the proteins can be used to indicate the date an animal was tagged, another can be used to indicate the laboratory that tagged the animal, and a third can be used to indicate the location where the animal was released. Claim 18 has been amended to clarify that one or more of albumin, lipoproteins, and gamma globulins can be used. Applicants submit that the amendments to the claims presented above meet the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request withdrawal of the rejection to claim 18 under § 112, second paragraph.

### Rejections Under 35 U.S.C. § 102

In numbered paragraph 14 on pages 5 and 6 of the Office Action, the Examiner rejected claims 7-9, 11, 12, 15, and 17 under 35 U.S.C. § 102(b) as being anticipated by Zarling et al. (U.S. Patent No. 5,674,698). Applicants respectfully traverse these rejections for the reasons presented below.

Independent claim 7 recites "an analysis target area within the uptake channel having a matrix therein, the matrix being activated by binding a capture molecule for the target molecule to the matrix." Independent claim 12 recites similar language.

Referring to FIG. 29 of the Zarling reference, the Examiner asserted on page 5 of the Office Action that Zarling teaches "a capture surface D9 within wick D2 (i.e. uptake channel having an analysis target area), wherein the capture surface comprises antibodies covalently linked to the inner surface of the tube wall, (i.e. matrix activated by binding a capture molecule to the matrix)." However, the activated matrix of the present invention differs from the capture surface D9 of Zarling.

In Zarling, the sample fluid D8 flows across the capture surface D9, and the target antigens bind to the antibodies present at the inner surface of the tube wall. The target antigens are captured only on the cylindrically-shaped inner surface of the tube wall. In contrast, in the present invention, the sample fluid flows **through** the activated matrix rather than across it. Because the activated matrix of the present invention is porous like a sponge, rather than cylindrical as in Zarling, the activated matrix of the present invention provides a greater surface area for capture than does the Zarling apparatus. Because the surface area for capture is greater in the present invention, the probability of capture and detection increases, which provides a more sensitive apparatus than the apparatus of Zarling.

In the present invention, the target molecules are captured throughout the entire matrix. In contrast, in Zarling, the target molecules are captured only on the inner surface of the tube wall, which is distanced from the center of the sample flowing therethrough. This distance reduces the likelihood of capture. Also, because the inner surface of the tube wall of Zarling is smooth, less turbulence is produced than that produced by the porous matrix of the present invention, which further reduces the likelihood of capture.

In addition, claim 12 recites "an analysis target area extending from an end of the uptake channel that is free of solid phase."

Unlike the present invention, the analysis target area of Zarling is not "free of solid phase." In Zarling, the target molecules accumulate on the inner surface of the tube wall of the capture surface D9. The capture surface D9 is positioned at the focal point of the diode laser D3. As shown in FIG. 29 of Zarling, the laser light must pass through the tube surrounding the capillary wick D2 to analyze the molecules on the capture surface D9. Thus, the analysis target area of Zarling is not free of solid phase.

In contrast, referring to FIG. 6A of the present invention, the analysis target area 156 does not contain an activated matrix. Rather, the analysis target area 156 is a bubble that contains the target molecules. As shown in FIG. 6C of the present invention, laser light is focused directly on the center of the bubble. Thus, the analysis target area of the present invention is "free of solid phase," as recited in claim 12.

An advantage of having an analysis target area that is free of solid phase is a more sensitive measurement. In Zarling, the laser light scatters as it passes through the wall of the

capillary wick D2, which creates background noise that interferes with the measurement of the capture surface D9. In contrast, in the present invention, there is no wall between the analysis target area and the laser light to interfere with measurement.

Thus, Applicants submit that independent claims 7 and 12 patentably distinguish over the prior art. Claims 8, 9, 11, 15, and 17 depend from the above-discussed independent claims and are patentable over the prior art for the reasons discussed above. The dependent claims also recite additional features not taught or suggested by the prior art.

For example, claim 15 recites “a tube connected to the side of the uptake channel to extend the uptake channel into the reservoir, wherein a bubble to be analyzed is formed on an end of the tube, the bubble comprising the analysis target area.” The bubble of Zarling is not similar to the bubble of the present invention. The bubble in Zarling is enclosed by the tube surrounding the capillary wick D2. In contrast, as shown in FIGs. 6A to 6C of the present invention, the bubble of the present invention is formed at the end of a tube that extends the uptake channel. While the bubble of the present invention is attached to the end of the tube, it is spaced from the inner walls of the tip, unlike the bubble of Zarling. Therefore, for at least this reason and the reasons set forth above with respect to claims 7 and 12, it is submitted that claims 8, 9, 11, 15, and 17 patentably distinguish over the prior art.

Therefore, Applicants submit that claims 7-9, 11, 12, 15, and 17 patentably distinguish over the prior art. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections of these claims under § 102.

#### Rejections Under 35 U.S.C. § 103(a)

In numbered paragraph 18 on pages 7 and 8 of the Office Action, the Examiner rejected dependent claim 10 under 35 U.S.C. § 103(a) as being unpatentable over Zarling in view of Wohlstadter et al (U.S. Patent No. 6,066,448).

In numbered paragraph 19 on pages 8 and 9 of the Office Action, the Examiner rejected dependent claim 18 under 35 U.S.C. § 103(a) as being unpatentable over Zarling in view of Ekong et al (Journal of Immunological Methods, 1995).

In numbered paragraph 20 on pages 9 and 10 of the Office Action, the Examiner rejected dependent claims 19 and 20 under 35 U.S.C. § 103(a) as being unpatentable over Zarling in view of Ekong, and further in view of Baars et al (Analytical Chemistry, 1999).

Applicants respectfully traverse these rejections for the reasons presented below.

Claims 10 and 18-20 depend from the above-discussed independent claims 7 and 12 and are patentable over the prior art for the reasons discussed above. Applicants also point out that a Declaration Under Rule 1.131 was submitted with the May 6, 2004 Response that indicates that the present invention was actually reduced to practice between September 1998 and March 1999, which precedes the publication date of the Baars article. Thus, Applicants submit the Baars article is not a valid prior art reference. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under § 103.

### Conclusion

In accordance with the foregoing, it is respectfully submitted that all outstanding objections and rejections have been overcome and/or rendered moot, and further, that all pending claims patentably distinguish over the prior art. Thus, there being no further outstanding objections or rejections, the application is submitted to be in condition for allowance, which action is earnestly solicited.

If there are any formal matters remaining after this response, the Examiner is requested to telephone the undersigned to attend to these matters.

Finally, if there are any additional fees associated with filing of this response, please charge the same to Deposit Account No. 502895.

Respectfully submitted,

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